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Inventors: Mathieu Hubertus M. Noteborn, Astrid Adriana A. M. Danen-van Oorschot, Jennifer Leigh Rohn

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Assignors: NOTEBORN, MATHIEU H. M. **Exec Dt:** 03/29/2001

DANEN-VAN OORSCHOT, ASTRID A.A.M. **Exec Dt:** 03/29/2001

ROHN, JENNIFER L. **Exec Dt:** 04/03/2001

Assignee: LEADD B.V.
WASSENAARSEWEG 72
LEIDEN, NETHERLANDS 2333

Correspondent: TRASK BRITT
ALLEN C. TURNER
P.O. BOX 2550
SALT LAKE CITY, UTAH 84110-2550

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Apoptin-associating protein

Abstract

The invention relates to the field of apoptosis. The invention provides novel therapeutic possibilities, for example novel combinatorial therapies or novel therapeutic compounds that can work alone, sequentially to, or jointly with Apoptin, especially in those cases wherein p53 is (partly) non-functional.

Inventors: **Noteborn, Mathieu Hubertus M.**; *(Leiderdorp, NL)* ; **Danen-van Oorschot, Astrid Adriana A. M.**; *(Berkel en Rodenrijs, NL)* ; **Rohn, Jennifer Leigh**; *(Amsterdam, NL)*

Correspondence Name and Address:
TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY
UT
84110
US

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Claims

1. An isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered.

2. The isolated or recombinant nucleic acid of claim 1 wherein said isolated or recombinant nucleic is derived from a cDNA library.

3. The isolated or recombinant nucleic acid of claim 2 wherein said cDNA library is a human cDNA library.

4. The isolated or recombinant nucleic acid of any one of claims 1 to 3 capable of hybridizing to a nucleic acid molecule encoding an Apoptin-associating proteinaceous substance as shown in SEQ ID NO 2 or SEQ ID NO 10.

5. The isolated or recombinant nucleic acid of any one of claims 1 to 4, wherein said isolated or recombinant nucleic acid is at least 60% homologous to the nucleic acid molecule of SEQ ID NO 1, SEQ ID NO 9, or SEQ ID NO 1 and SEQ ID NO 9.

6. A vector comprising an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered.

7. The vector of claim 6 wherein said vector comprises a gene-delivery vehicle.

8. A host cell having an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered.

9. The host cell of claim 8 wherein said cell is a eukaryotic cell.

10. An isolated or recombinant Apoptin-associating proteinaceous substance comprising a sequence as shown in SEQ ID NO 2 or SEQ ID NO 10 or a functional equivalent or functional fragment thereof capable of causing apoptosis in a cell to which said proteinaceous substance has been administered.

11. The proteinaceous substance of claim 10 encoded by the nucleic acid of any one of claims 1 to 5.

12. The proteinaceous substance of claim 10 or claim 11, said proteinaceous substance comprising at

least a part of an amino acid sequence as shown in SEQ ID 2 or SEQ ID 10 or a functional equivalent or functional fragment thereof.

13. An isolated or synthetic antibody specifically recognizing a proteinaceous substance or functional equivalent or functional fragment thereof of any one of claims 10 to 12.

14. A proteinaceous substance specifically recognizable by an antibody according to claim 13.

15. A method of inducing apoptosis in a cell comprising administering to said cell an apoptosis inducing substance selected from the group consisting of: an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, a vector comprising an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, a host cell transformed with an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, an isolated or recombinant Apoptin-associating proteinaceous substance comprising a sequence as shown in SEQ ID NO 2 or SEQ ID NO 10 or a functional equivalent or functional fragment thereof capable of causing apoptosis in a cell to which said proteinaceous substance has been administered, and mixtures thereof.

16. The method according to claim 15 wherein said apoptosis is p53-independent.

17. A pharmaceutical composition for use in a subject, said pharmaceutical composition comprising: a pharmaceutically acceptable amount of a component selected from the group consisting of: an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, a vector comprising an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, a host cell transformed with an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, an isolated or recombinant Apoptin-associating proteinaceous substance comprising a sequence as shown in SEQ ID NO 2 or SEQ ID NO 10 or a functional equivalent or functional fragment thereof capable of causing apoptosis in a cell to which said proteinaceous substance has been administered, and mixtures thereof, said component together with a pharmaceutically acceptable carrier, acceptable and compatible for said subject and said component.

18. The pharmaceutical composition of claim 17 wherein said further comprising: a nucleic acid

encoding Apoptin or a functional equivalent or fragment thereof or Apoptin or a functional equivalent or fragment thereof.

19. A method for treating a subject having a disease wherein enhanced cell proliferation or decreased cell death is observed, said method comprising treating the subject with the pharmaceutical composition comprising: a pharmaceutically acceptable amount of a component selected from the group consisting of: an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, a vector comprising an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, a host cell transformed with an isolated or recombinant nucleic acid of SEQ ID NO 1 or SEQ ID NO 9 or a functional equivalent or functional fragment thereof, said functional equivalent or functional fragment thereof encoding an Apoptin-associating proteinaceous substance capable of causing apoptosis in a cell to which said isolated or recombinant nucleic acid or Apoptin-associating proteinaceous substance has been delivered, an isolated or recombinant Apoptin-associating proteinaceous substance comprising a sequence as shown in SEQ ID NO 2 or SEQ ID NO 10 or a functional equivalent or functional fragment thereof capable of causing apoptosis in a cell to which said proteinaceous substance has been administered, and mixtures thereof, together with a pharmaceutically acceptable carrier, acceptable for said subject and said component to induce apoptosis.

20. The method according to claim 19 wherein said disease comprises cancer or auto-immune disease.

21. The method according to claim 19 wherein said apoptosis is p53-independent.

Description

TECHNICAL FIELD

[0001] The invention relates generally to the field of biotechnology and medicine, and more particularly relates to methods and associated means for inducing apoptosis in a cell.

BACKGROUND

[0002] Apoptosis is an active and programmed physiological process for eliminating superfluous, altered or malignant cells (Earnshaw, 1995, Duke et al., 1996). Apoptosis is characterized by shrinkage of cells, segmentation of the nucleus, condensation and cleavage of DNA into domain-sized fragments, and is then generally followed by internucleosomal degradation. The apoptotic cells fragment into membrane-enclosed apoptotic bodies. Finally, neighboring cells and/or macrophages will rapidly phagocytose these dying cells (Wyllie et al., 1980, White, 1996).

[0003] Cells grown under tissue-culture conditions and cells from tissue material can be analyzed for being apoptotic with agents staining DNA, as e.g. DAPI, which stains normal DNA strongly and regularly, whereas apoptotic DNA is stained weakly and/or irregularly (Noteborn et al., 1994, Telford et al., 1992).